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4.

A CASE OF CALCIFICATION OF THE ARTERIES AND OBLITERATIVE ENDARTERITIS, ASSOCIATED WITH HYDRONEPHROSIS, IN A CHILD AGED SIX MONTHS.

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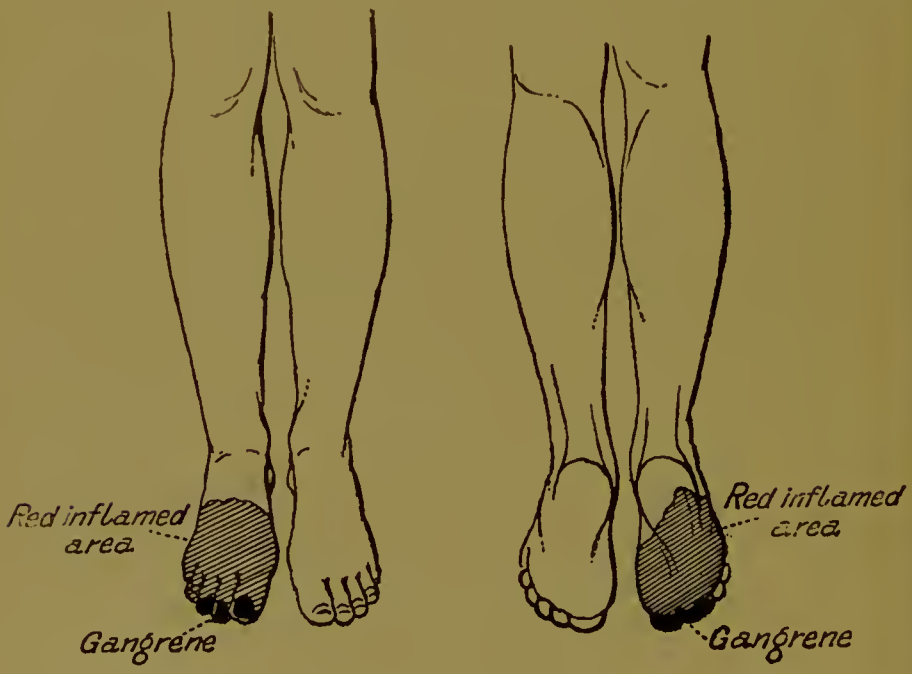
E. S., æt. 6 months, was admitted under the care of Dr. Hale White, on May 11th, 1899, for general debility and wasting. He was born and had always lived at Camberwell. He was fed from the breast for the first two months, and after this, on account of his mother suddenly ceasing to lactate, was brought up on cow's milk and Robb's food biscuits. For the week prior to admission he had been given Nestlé's food. He was the second child in fourteen months. The first child was premature and still-born. The labour was difficult, it being necessary to administer chloroform. He was described by the mother as being "a beautiful baby and big enough for two." For the last three months he had lost weight and had grown very feeble. He would lie for hours without making a noise, and seemed to be too weak to cry. He was very constipated, but was never sick. No further history of any illness could be obtained.

Condition on admission.—Pulse 96; Temperature 97·6°. He was a miserable emaciated looking baby, lying very still and not resisting examination. There was no hair, but the scalp was covered with a scaly scurf. The head appeared to be very flat behind. The chest was not rachitic, a few rhonchi could be heard at the bases, otherwise the chest was normal. The cardiac impulse could not be seen nor felt. The heart-sounds were rapid; there were no adventitious sounds. On May 15th he vomited. On May 20th he had diarrhœa and sickness and was very feeble. He weighed 3·325 kilos. (8 lbs. 4 ozs.); May 27th he weighed 3·2 kilos. (8 lbs.). June 3rd.—During the previous week he did not suffer from much diarrhœa or vomiting. June 6th he was more feeble, and still suffered from sickness. His right foot was very cold and was rapidly becoming black. On the 8th, 10th, 12th and 13th the report states he was about the same. On the 19th he refused food. The foot was very hard and inflamed. On the 20th the foot

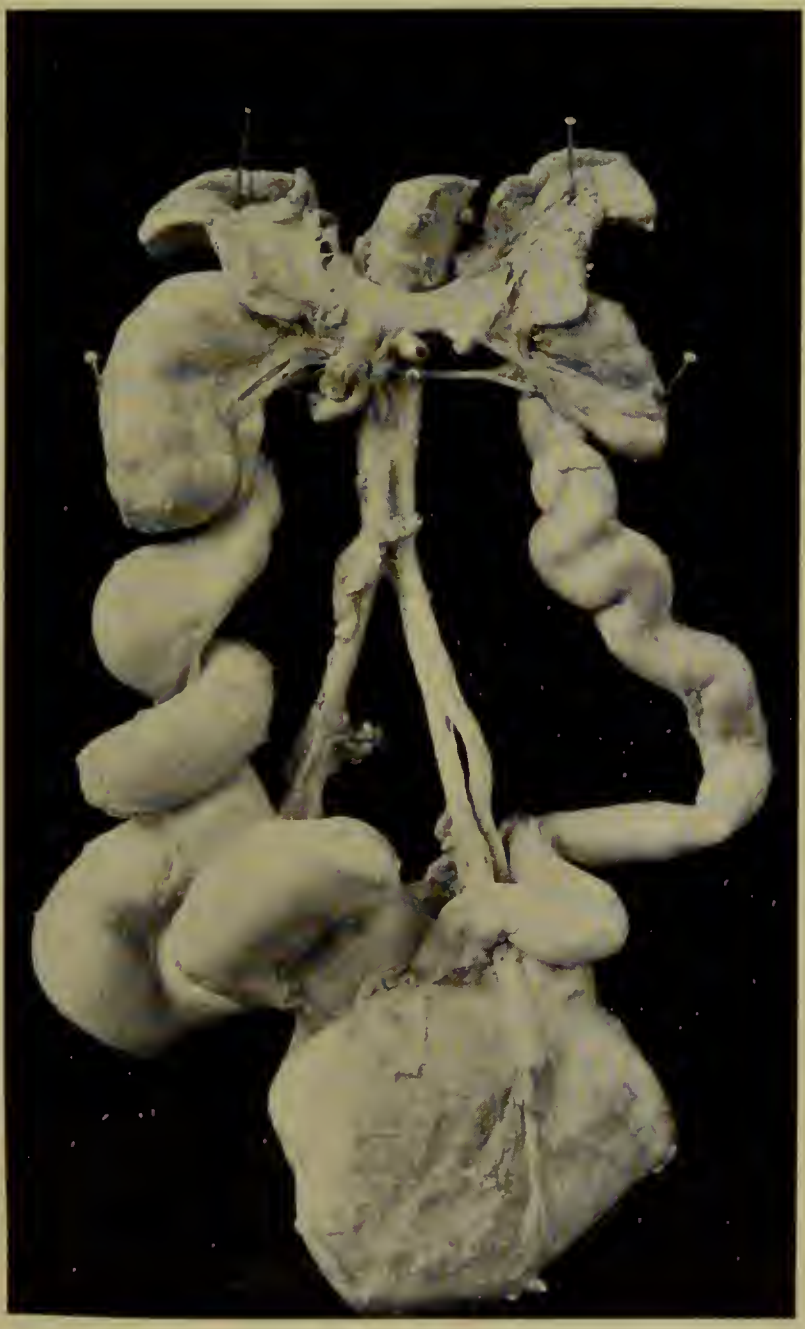


was black and gangrenous in appearance. He was very much worse, and died at 4.30 p.m. on the 21st.

The necropsy was performed on June 21st, 1899, ten hours after death. There were no signs of decomposition. Rigor mortis was well marked. The body was very emaciated. There were no external signs of congenital syphilis. The toes were becoming gangrenous (*vide* diagram). The skin was shrivelled and had a dead black appearance. On the sole and dorsum of the right foot a red and inflamed looking area of skin was seen (*vide* diagram). The femoral artery could be felt as a thick and firm cord. The brain was healthy in appearance and all the cerebral vessels appeared quite normal. The cervical glands were not enlarged. The thyroid was healthy; the thyroid arteries were rigid, thickened, hard and nodular, and their lumina were much narrowed. There was no pleurisy. Several very small nodules could be felt in both lungs. On section they proved to be tubercles arranged in small groups of five or six. The larynx, trachea and bronchi were healthy. The bronchial glands were enlarged and caseous from recent tuberculous changes. There was no pericarditis. There was no fat on the surface of the heart. The coronary arteries were thickened, tortuous and hard, and their lumina were much narrowed. The right ventricle was slightly thicker than normal; there was no dilatation. The valves and endocardium were normal. The left ventricle and auricle were normal in appearance; they were not dilated, and the myocardium appeared to be normal. The endocardium of the left auricle at, and just above the attachment of the mitral valve was hard, thickened, nodular and gritty. This was particularly well marked on the posterior and outer parts of the auricle. The gritty nodules were very small and were arranged in lines in the long vertical axis of the auricle. A similar condition was found in the endocardium lining the left ventricle, especially in the lower part over the musculi papillares. The pulmonary arteries were a little thickened and a few small yellowish patches were found in the intima of some of the medium sized branches. The intima of the aorta just above its origin up to about 1 to 2 millimetres above the level of the free edges of the valves was rough and irregular and had a feeling of grittiness. The remainder of the aorta had a normal appearance and feeling,

with the exception of the last two centimetres, which felt thickened. The intima presented a large number of small light greenish yellow spots and patches which also felt hard and gritty. The iliac arteries were very much thickened and felt firm, hard and rigid, like pipe stems. The lumina were much narrowed, in fact almost obliterated. The external and internal iliac arteries on both sides were similarly affected, but the vessels on the right more than those on the left. The intima presented a yellowish, shiny, glazed, or rather varnished appearance; it felt hard and brittle, and when bent cracked with ease. A transverse section showed much narrowing of the lumen which gave the impression that it had been caused by a thickening of the tunica media. On the whole, the appearance resembled atheroma rather than primary calcification. Both the femoral arteries and their branches were affected in a similar manner, the right, however, more so than the left. The small arteries of the lower part of the legs and the feet were almost obliterated, especially the right *anterior dorsal* and the right external plantar. The brachial artery and its branches, the thyroid, the mesenteric, hepatic and renal arteries were all thickened and rigid and showed changes similar to those described above. The stomach and the intestine had a normal appearance. There was no peritonitis and no ascites. The liver appeared to be normal, except for the hepatic arteries, which were thickened, hard, rigid, somewhat nodular and narrowed. The gall-bladder, pancreas and lymphatic glands were healthy. The spleen contained a number of small tubercles; the splenic arteries were affected in the same way as the arteries already described. The suprarenal arteries were also affected. The left kidney measured 3 centimetres in length; it felt as if it was hollowed out; its pelvis was much dilated. The right kidney measured 4·2 centimetres in length; it was much firmer than the left, but it also felt as if it was hollowed out, and its pelvis was also dilated; in fact both were in a condition of hydronephrosis, although not enlarged. Both ureters were very much dilated and were extremely tortuous; the right was much more dilated than the left and was as large as a piece of the small intestine, in fact, after the intestines had been removed in the usual manner by the

A Case of Calcification of the Arteries and Obliterative Endarteritis, associated with Hydronephrosis, in a child aged six months.



Photograph showing hypertrophied bladder, dilated ureters, and calcified arteries.

post-mortem room attendant, it was thought, on looking at the peritoneal cavity, that he had left some of the intestine behind. In its most dilated part the right ureter measured 6·5 centimetres in circumference, the left 4 centimetres. The bladder was much hypertrophied, and was also dilated; just above the neck the wall measured 5 millimetres in thickness. Neither of the ureters were obstructed. The urethra itself was not dilated. There was a very marked degree of phimosis, the urine having to pass through an orifice no larger than a pin-prick.

Microscopical Examination.—Sections of the right anterior tibial artery, and of the kidney were prepared by Dr. Stevens, and we are also indebted to him for the drawings of the microscopical appearances of these structures. The specimens were stained with eosin and hæmatoxylin.

The anterior tibial artery was selected as it was markedly affected. When examined with the low-power (Zeiss A, eye-piece, 1), the following main features could be made out.

1. The lumen was much narrowed and was almost entirely occluded by an organising ante-mortem thrombus.

2. The intima was enormously thickened, being quite five or six times wider than normal.

3. The elastic lamina was very distinct, it was intact, and was not so crinkled in appearance as in a normal artery.

4. There was well marked calcification, especially of the tunica media.

5. There was loosening of the tunica adventitia.

6. There was thickening of the vasa vasorum.

Examined under a higher power (Zeiss D) the lumen of the vessel was seen to be much narrowed, and it was almost filled with an organising ante-mortem thrombus. In two places (*vide* fig. 3), the epithelial layer of the intima was separated from the adjacent subendothelial layer by a portion of the organising thrombus, otherwise the innermost endothelial layer appeared to be normal. The main thickening of the artery was due to a marked proliferation and increase in size of the subendothelial layer of the intima, the tissue forming which presented a markedly

degenerated appearance, it being very granular-looking, and containing few nuclei. Immediately adjacent to the elastic layer or fenestrated membrane of Henle, there was a continuous ring of calcareous degeneration, which had stained a deep bluish violet with hæmatoxylin; it presented a somewhat hyaline and granular appearance. It varied very considerably in thickness, in places it was thin, whereas in others it occupied nearly one-half of the thickness of the subendothelial layer. Between the markedly calcified outer zone of the subendothelial layer and the degenerated inner portion, several small, rather dark brownish-looking spots and areas of what appeared to be granular debris were seen. The elastic layer or fenestrated membrane of Henle showed up as a bright, clear, continuous yellow line. It was intact, and was much less crinkled than usual. The tunica media showed extensive degenerative changes and calcification, quite the inner five-sixths of it being involved, and it was stained a deep bluish violet, with the hæmatoxylin just as the outer part of the subendothelial layer of the intima. It also presented a somewhat hyaline and granular appearance. Externally, it was bounded by a thin, more deeply-stained zone. In some parts of the artery it was bounded by a thin layer of involuntary muscular fibres, with long, well-stained nuclei, varying in thickness from one or two, to ten or twelve muscle fibres lying parallel to each other. This condition is well represented in the drawing. In the inner degenerated zone only a few small, scattered, faintly-stained nuclei could be seen, nearly the whole of this part having undergone extensive calcareous degeneration, and nowhere in this degenerated part could the outline of any individual muscular fibres be made out.

The tunica adventitia did not show any definite morbid changes. There did not appear to have been any periarteritis. There was no cellular infiltration. The connective tissue seemed to be loosely arranged; but there was no evidence of any marked degenerative changes. The vasa vasorum were a little thickened; they were not thrombosed.

The Kidneys.—The fibrous capsules were considerably thickened. The most marked change was the general dilatation of the tubules.

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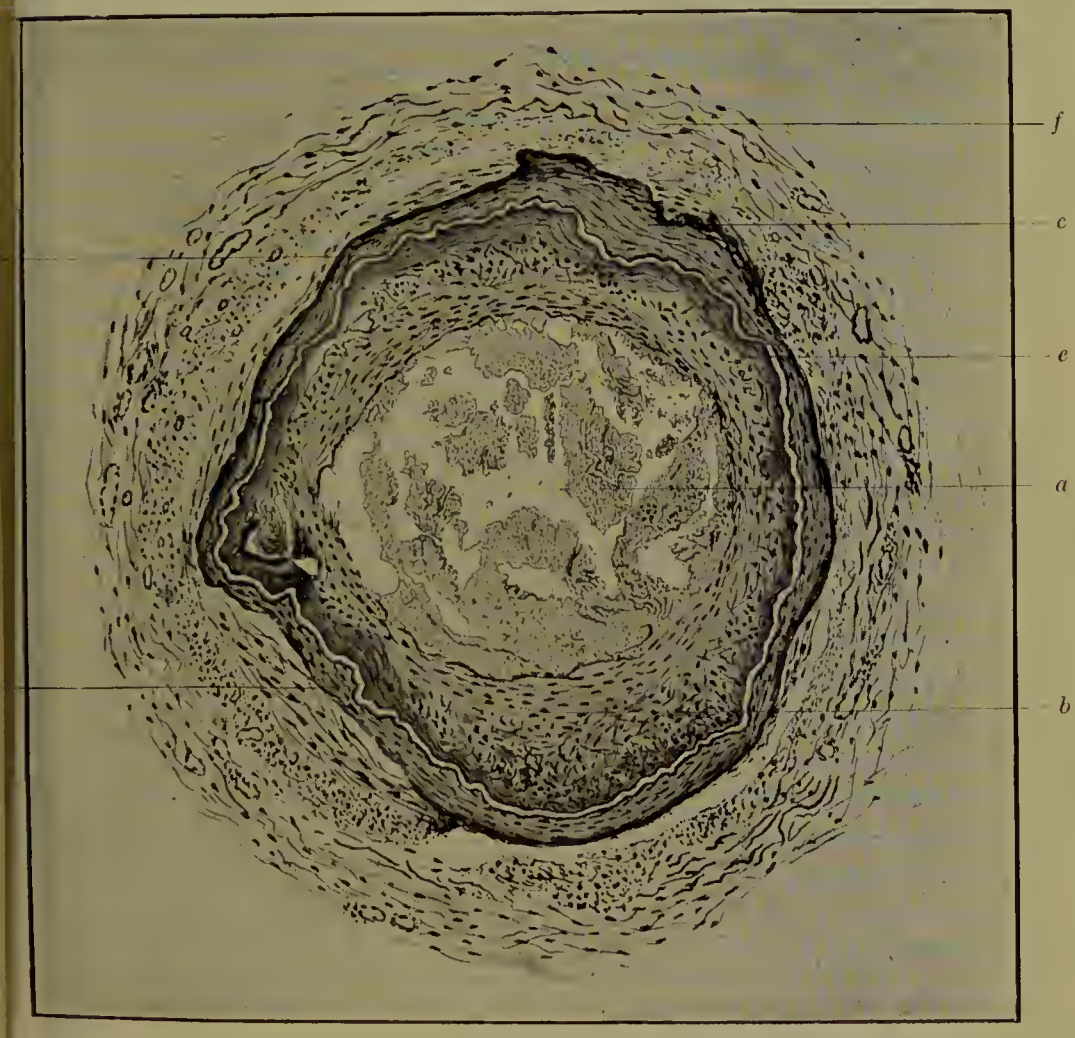

Thos. G. Stevens (del.)

a. Ante-mortem thrombus.
b Thickened tunica intima.
c. Calcified tunica intima and media.
d. Muscle of tunica media.
e. Fenestrated membrane of Henle.
f. Tunica adventitia.

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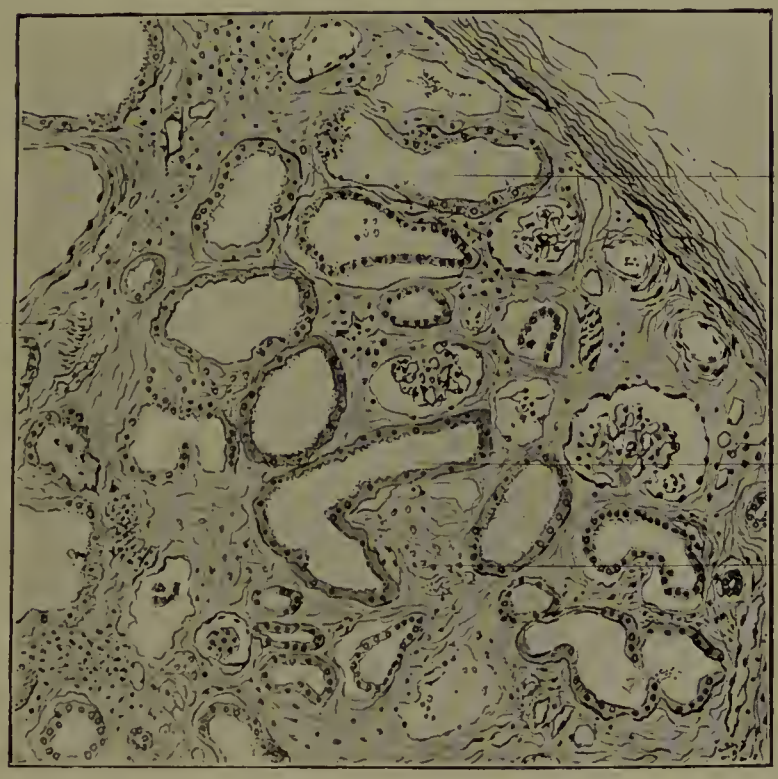

THOS. G. STEVENS (del.)

a. Dilated renal tubule.
b. Increased growth of fibrous tissue
c. Thickened arteriole.

Most of them were lined by epithelium, which appeared to be stretched and flattened, the individual cells being much elongated and very little deeper than the diameter of their nuclei. In some of the tubules the cells were so flattened that the nuclei were compressed, and were altered from their normal circular to an oval shape. In a good many of the tubules the epithelium had separated from the subepithelial layer. Some of the tubes which were most dilated had no lining of epithelial cells; but contained a few epithelial cells lying loose in the centre of their dilated lumina. The epithelium of a few of the tubules had a markedly granular appearance, the nuclei of some of these cells being invisible, and very faintly stained in others. The glomerular capsules were markedly dilated. The glomeruli themselves were healthy in appearance. In places there was a very marked increase in the amount of interstitial connective tissue. Several sections were examined, and all the arteries, even to the smallest arterioles showed a remarkable amount of thickening, as much, if not more, than is usually seen in an advanced case of chronic interstitial nephritis.

Remarks.—There are many points of interest to be considered in this remarkable and, as far as we know, unique case. First of all there is the condition of hydronephrosis, dilated ureters and hypertrophied bladder; secondly the advanced general arterial degeneration and calcification which had led to gangrene of the toes; and lastly the ætiology of these two conditions and their relation, if any, to each other.

Hydronephrosis in children is probably almost always due to some obstruction to the passage of the urine in the ureter, bladder, urethra or prepuce, but often the precise nature of the obstruction cannot be made out. Of ten cases collected by Holt[1], in only three was a sufficient degree of obstruction found. In our case both kidneys were involved, both ureters were markedly dilated, and the bladder was much hypertrophied, so that the obstruction must have been in the urethra or prepuce. The urethra was not dilated. The prepuce, however, was very tight, and could not be drawn over the glans penis for any distance. It required a very

[1] Holt. Diseases of Infancy and Childhood, p. 608.

careful examination to find the preputial opening, and it was only discovered when an attempt was made to draw the prepuce over the glans. It was a minute opening, about the size of a pin-prick, and this tiny orifice was the only one through which the urine could have passed. Such a condition must have caused a good deal of difficulty to the passage of urine. The prostate was not enlarged and there was no vesical calculus. So it appeared that the phimosis was the cause of the hypertrophied bladder, dilated ureters, and hydronephrosis, for it was the only obstruction found. Against this view was the fact that the urethra was not dilated, and also that phimosis is comparatively common and hydronephrosis very rare. In our case, however, the phimosis was extreme. We have already mentioned that occasionally no obstruction is detected, and we have found such a case recorded by Courvelain. (Bull. et Mem. de la Soc. Anat. de Paris, March, 1900). The bladder of the fœtus was so distended and its abdomen so swollen in consequence, that puncture was necessary before delivery could be effected. Five hundred and fifty grammes of clear, lemon yellow, highly albuminous fluid was withdrawn. The child was a female and weighed 2·835 kilogrammes. The abdominal distension of the child was found to have been due to retention of urine. The ureters and the renal pelves were dilated. No malformation, calculus, or stricture was found. Similar cases are mentioned in this paper as having been recorded by Gaüdon, Cornelli, and Lefour. Porak has reported a case in which the obstruction was found to be due to a valvular fold in the mucous membrane, a condition which may possibly exist in other cases but may easily be overlooked.

In two of Holt's cases the ureters were so large as to be mistaken for coils of small intestine, as in our case. Not only do the ureters in these cases resemble a coil of small intestines, in size, but also in their appearance of thinness and semi-translucency; they are also, as a rule, much elongated, sacculated and twisted, which condition can be well seen in the photograph of our case. (Fig. 2).

In two of Holt's cases "typical examples of the atrophic form (contracted kidney) were seen." One of these children died at

the age of one month. In our case there was little kidney substance left, and a microscopical examination of it showed dilated tubules, interstitial fibrosis and thickening of the arteries such as is seen in chronic interstitial nephritis, a condition we shall have to again consider when discussing the pathology of the general arterial degeneration. One of Holt's cases was remarkable; the child died of what appeared to be marasmus. Double hydronephrosis was found, and the ureters were much dilated, measuring three fourths of an inch in diameter. The right kidney had an adherent capsule and was very nodular on the surface. In the cortex, just beneath the capsules, there were several small cysts containing pus. The left kidney was in a condition of hydronephrosis the cortex being very thin. Microscopical examination showed chronic diffuse nephritis of the atrophic variety; the capsule of the right kidney was much hypertrophied and there were several small abscesses beneath it in the cortex, the rest of this kidney was converted into dense fibrous tissue. The walls of the bladder were much hypertrophied. The urethra and prepuce were normal. No mention is made in any of these cases of degenerative changes in the arteries.

Another point of interest in our case is the consideration of the time at which the change commenced. The above mentioned cases show that the hypertrophy of the bladder, dilated ureters, and hydronephrosis may be brought about in utero, and we are of opinion that taking into consideration the very marked changes in our case that its origin must have been congenital.

We now pass on to the consideration of the pathology of the changes which were found in the arteries. These were extreme and had led to gangrene as a result of obliteration or great narrowing of their lumina, in fact, the case may be described as senile gangrene occurring in a child six months old. To briefly recapitulate these changes; there was enormous thickening and calcification, which rendered the vessels hard and rigid like pipe-stems, so that on bending them they would snap with a crack. The microscope showed enormous thickening of the intima with calcareous degeneration in this layer, and also calcareous degeneration

involving nearly the whole of the media, changes more compatible with a patient eighty years of age than a baby of six months.

In addition to this calcareous degeneration of the arteries, two other marked pathological changes were found, each of which would well account for the death of the child, viz., the hydronephrosis and atrophic fibroid condition of the kidneys, and the acute tuberculosis of the lungs and spleen. Naturally the first question which arises is—Was the arterial degeneration secondary to either of these conditions? We do not think the tuberculosis had anything to do with it. This was probably a late infection predisposed to by the emaciated condition of the child and may be looked upon as the actual cause of death. There were no old foci of tubercular disease, and it was evident that the extensive changes in the arteries were of much older date than the tuberculosis, which was obviously quite recent.

With regard to the renal condition, we do not consider that it was adequate to account for such very marked arterial changes. We have never seen, even in an adult, such marked degenerative changes as a result of advanced chronic interstitial nephritis or hydronephrosis, and we have not been able to find a single case recorded of such extensive arterial degeneration in children in association with either chronic nephritis or hydronephrosis.

The arteries really presented the changes not only of what might be expected in an advanced condition of chronic interstitial nephritis, but also the primary calcification of the tunica media, which is associated with old age.

The calcification of the endocardial lining of the left auricle and ventricle was also quite different in appearance to the patches of atheroma which are sometimes found in the endocardium covering the mitral valve in cases of advanced chronic nephritis.

That the change was something more than a primary calcification is also evident, for in the primary calcification of the medium-sized vessels, which occurs in old people, the tunica media is the part which is involved, it becoming first fatty, and then calcareous, until this coat may be represented entirely by a brittle calcareous tube. The intima and adventitia are, as a rule, very little, if at all affected. In our case there was remarkable thickening of the

tunica intima, which makes it quite clear that the morbid process was something more than a mere primary calcification.

The remarkable thickening of the tunica intima, which may be described as quite five or six times wider than a normal intima, certainly points to syphilis as a possible cause, for syphilis is certainly more likely to cause an obliterative endarteritis than any other disease, although marked thickening may occur in cases of chronic interstitial nephritis.

There certainly was no positive evidence of congenital syphilis; we examined all the other organs histologically and found no evidence, with the exception of the changes in the arteries. The liver was examined particularly, but it showed no sign whatever of intercellular cirrhosis. There is perhaps one point in the family history which is suggestive of syphilis, and that is, the mother was delivered prematurely of a still-born child fourteen months before the birth of this child.

The degree of the arterial degeneration pointed to a commencement of the disease in utero, another point which we consider to be in favour of a syphilitic origin.

Both endarteritis and atheroma are acknowledged results of syphilis, but such marked general calcification is unusual, and we are inclined to look upon the arterial changes, as being due to more than one cause. We consider that without much doubt syphilis was the main factor, but that the hydronephrosis and chronic fibroid changes in the kidneys played their part by raising the general arterial tension. The calcification we look upon as showing an extraordinary tendency of the tissues to early degeneration, but consider that it must be looked upon as a secondary condition.

Durante (Bull. de la Soc. Anat., January, 1899, and Epitome B. M. J., vol. 1, 1899, No. 542) records a case of "congenital atheroma." The patient was a seven months' child, and was seen fourteen days after birth. It was suffering from general œdema, redness of the skin and periumbilical lymphangitis. Death resulted from peritonitis. At the post-mortem examination the organs were found healthy, with the exception of the peritonitis, The thymus was small and pale. There was no pericarditis nor

valvular disease. The pulmonary artery presented a hard condition of its walls, with here and there patches of considerable density, similar to the appearance usually seen in a senile aorta. These hard plaques broke when they were bent. The internal surface of the vessel was white, but was quite smooth. There were no naked-eye changes in the aorta; but it felt more rigid than normal. Microscopically the pericardium, endocardium and myocardium were found to be healthy. The tunica media of the pulmonary artery showed fatty degeneration and calcareous infiltration, the inner part of the coat was mainly affected, the muscular fibres in the outer part of the coat appearing to be fairly normal. In other parts of the vessel the middle coat showed only a little fatty degeneration, and in places the neighbouring cells of the inner coat were involved. Similar changes, but to a much less degree, were found in the aorta. In none of the vessels was there any appearance of endarteritis. He looked upon it as congenital, the lesion being too marked to have developed so soon after birth. No details could be ascertained as to the health of the parents. Probably one or both were syphilitic.

The changes recorded in the above case were not so advanced as in our case, for the only obvious lesions were in the pulmonary arteries. The tunica media was mostly involved, and it was definitely stated that there was no appearance of endarteritis in any of the vessels.